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13. ABSTRACT *(Maximum 200 Words)*

Several studies have suggested that telemedicine techniques may be used to screen patients for signs of diabetic retinopathy. The objective of this research is to use nonmydriatic digital fundus cameras to collect retinal images at remote sites that can be transmitted and interpreted by an ophthalmologist. The present study has examined the validity of using digital fundus images to recognize the presence and extent of retinopathy in diabetic patients. Nonmydriatic, nonstereoscopic digital fundus images were reviewed for signs of diabetic retinopathy and results were compared with those of clinical examination of the same patients. Thirty patients (57 eyes) have been examined to date. Seven were found to have image quality too poor to evaluate. Poor image quality was attributable to dense cataracts, miotic pupils or total retinal detachment. Interpretation of fundus by digital image and clinical ophthalmoscopy showed consistent results in recognition of diabetic retinopathy (k=0.65 (95% CI 0.42-0.83)); macular edema (k=0.88 (95% CI 0.64-1.11)) and follow-up recommendations (k=0.61 (95% CI 0.31-0.90)). These preliminary results suggest that digital fundus images may accurately recognize diabetic retinopathy.

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Introduction

Several recent studies have suggested that evaluation of nonmydriatic fundus photographs provide a cost-effective alternative for screening large numbers of patients for diabetic retinopathy (Ref 1,10,11,12,14,16,17). We propose to expand upon this method by using digital photographic images of the fundus, which can be taken, at the outpatient clinic, transmitted over telephone lines and accessed at a remote computer terminal by an ophthalmologist. This would provide prompt assessment by a specialist with minimal cost. One objective of the proposed study is to determine if digital imaging of fundus photographs can serve as a consistently reliable method for detection of high-risk diabetic retinopathy, which requires immediate treatment or close surveillance. It is hoped that such a method for could serve as a cost-effective option for screening of retinopathy in large population of diabetic patients. This technique would also allow an ophthalmologist to examine the eyes of a patient who resides at a distant site promptly and without the need for travel. Such benefits would be extremely useful for the delivery of optimal and cost-effective medical care to soldiers and their families assigned at locations far from a military medical center.

Body

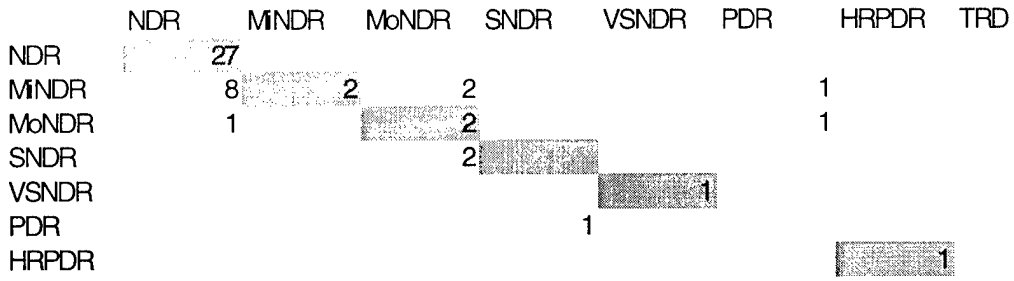
This protocol was delayed in its start time due to problems with procurement and operation of hardware used in acquisition and transmission of digital images. The vendor was able to establish an operational system for data collection in March 2002.

Thirty patients have been enrolled in this study to date: 20 male subjects (eleven African-American and nine Caucasian) and 10 female subjects (six Caucasian, three African-American and one Asian). The average age of the participants is 64 years. Three eyes were excluded from the study as a result of having had eye surgery during the past year. The prevalence of diabetic retinopathy (determined by clinical exam) among the study group was 28% and the prevalence of macular edema was 8%. These prevalences are similar to those reported in several studies (Ref 2,15,18).

Single nonmydriatic, nonstereoscopic digital fundus images were considered gradable by the interpreter in fifty of the fifty-seven images that were reviewed. Poor image quality correlated with physical findings limiting view of the fundus in all seven cases; surgical grade cataracts in four cases, miotic pupils in two cases and a total retinal detachment in the other case.

The following tables display the level of agreement in comparing the results of clinical examination and digital image examination: kappa statistic used to assess nominal agreement not attributed to chance (Ref 3,13)

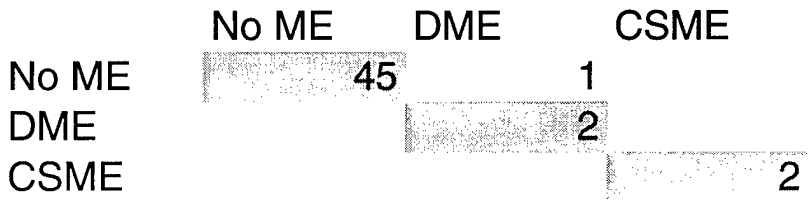
A. Level of Agreement for Diabetic Retinopathy:
   X-axis impression from clinical exam; Y-axis impression from digital image review



NDR= no diabetic retinopathy; MiNDR = mild nonproliferative diabetic retinopathy; MoDR=moderate nonproliferative diabetic retinopathy; SNDR=severe nonproliferative diabetic retinopathy; VSNDR- very severe nonproliferative diabetic retinopathy; PDR=proliferative diabetic retinopathy; HRPDR=high-risk proliferative diabetic retinopathy and TRD= traction retinal detachment. Definitions of these categories or described in the appendix and in references 4-9.

Unweighted kappa = 0.65 $\pm$ 0.1 with 95% CI 0.42 to 0.83
Sensitivity = 0.74
Specificity = 0.71

B. Level of Agreement for Diabetic Macular Edema
X-axis impression from clinical exam; Y-axis impression from digital image review



ME= No macular edema; DME= diabetic macular edema, not clinically significant; CSME= Clinically Significant Macular edema

Unweighted kappa= 0.88 $\pm$ 0.12 with 95% CI 0.64 to 1.11
Sensitivity = 1.0
Specify = 0.98

C. Level of Agreement for Follow-up Recommendations
X-axis impression from clinical exam; Y-axis impression from digital image review

	12 mos	6 mos	4 mos	1 mo	FA/Laser
12 mos	36	5	0	0	0
6 mos	1	1	0	0	0
4 mos	1	0	2	0	0
1 mo	0	0	0	0	0
FA/laser	0	0	0	0	4

Mos = months until next recommended follow-up exam
FA/laser= fluorescein angiogram and /or macular laser treatment in less than one Month.

Unweighted kappa = 0.61 $\pm$ 1.1 with 95% CI 0.31 to 0.90
Sensitivity = 0.95
Specificity = 0.58

Key Research Accomplishments:

- Preliminary results show that review of a single nonmydriatic, nonstereoscopic digital fundus image can recognize diabetic retinopathy at a level consistent with that of clinical ophthalmoscopic examination

- Preliminary results show that review of a single nonmydriatic. nonstereoscopic digital fundus image can recognize diabetic macular edema at a level consistent with that of clinical ophthalmoscopic examination

Reportable Outcomes:

- Presentation of results at Society of Military Ophthalmology Biennial Conference, Bethesda, MD, March 2002

- Submission of abstract for The Association for Research in Vision and Ophthalmology Conference 2003

Conclusions:

The initial results of this study suggest that processing and interpreting of digital fundus images may be a valid method for screening diabetic retinopathy using telemedicine techniques. Greater enrollment of subjects is necessary to achieve the desired statistical power that would support these preliminary results.

These results are ascertained using a single fundus image for analysis. Similar results in level of agreement have been reported with a similar number of subjects using stereoscopic imaging, a proprietary imaging system and composite results from a collection of five images of different regions of each fundus that was examined (2). This report is the only study found in a Medline Search from 1966 to present (search words: diabetic retinopathy AND digital OR telemedicine) that attempted to ascertain the validity of using digital fundus images to assess diabetic retinopathy.

In the present study, digital fundus images are collected using a commercially available nonmydriatic camera and fundus imaging equipment that is currently used for fluorescein angiography in several military ophthalmology clinics. Such resources would make it practically feasible to implement these techniques for screening diabetic retinopathy in

the military ophthalmology setting should it be considered advantageous to use this information for that purpose.

The investigators in this study have no financial interest any of the equipment used in this study.

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Appendix

Levels of Retinopathy (Modified from ETDRS)

1. Nonproliferative Diabetic Retinopathy (NPDR)
    a. Mild NPDR

i) At least 1 hemorrhage/microaneurysm
ii) Definition not met for b,c or d below
iii) Further subclassification: No Macular Edema, Diabetic Macular Edema-not clinically significant and Clinically Significant Macular Edema

b. Moderate NPDR
i) H/Ma > standard photograph 2A (ref 6) OR
ii) Cotton Wool Spots (CWS) , venous beading (VB) or Intraretinal Microvascular Abnormalities (IRMA) definitely present but not at level seen in c or d below
iii) Further subclassification: No Macular Edema, Diabetic Macular Edema-not clincally significant and Clinically Significant Macular Edema

c. Severe NPDR
i) H/Ma > standard photograph 2A (ref 6) in all four quadrants of photograph OR
ii) VB in two or more quadrants of photograph OR
iii) IRMA > standard photograph 8A (ref 6)
iv) Further subclassification: No Macular Edema, Diabetic Macular Edema-not clinically significant and Clinically Significant Macular Edema

d. Very Severe NPDR
i) Any two or more from c above
ii) Further subclassification: No Macular Edema, Diabetic Macular Edema-not clinically significant and Clinically Significant Macular Edema

2. Proliferative Diabetic Retinopathy

a. Early PDR
i) Neovascularization of the Disc (NVD) or Elsewhere (NVE)
ii) Definition not met for b below
ii) Further subclassification:
1) Macular Edema: No Macular Edema, Diabetic Macular Edema-not clincally significant and Clinically Significant Macular Edema
2) Traction Retinal Detachment (TRD): Not threatening fovea, Threatening fovea

a. High-Risk PDR
i) NVD > standard photograph 10A (Ref 6) OR
ii) Any NVD with vitreous hemorrhage OR
iii) NVE > 1/2disc area with vitreous hemorrhage OR
iv) Further subclassification:
1) Macular Edema: No Macular Edema, Diabetic Macular Edema-not clinically significant and Clinically Significant Macular Edema
2) Traction Retinal Detachment (TRD): Not threatening fovea, Threatening fovea

a. Regressed PDR

i) Fibrous Proliferation at Disk or Elsewhere
ii) Further subclassification:
1) Macular Edema: No Macular Edema, Diabetic Macular Edema-not clincally significant and Clinically Significant Macular Edema
2) Traction Retinal Detachment (TRD): Not threatening fovea, Threatening fovea

Clinically Significant Macular Edema:

a. Thickening of the retina <500 um from the center of the macula OR
b. Hard exudates with thickening of the adjacent retina located < 500 um from the center of the macula OR
c. A zone of retinal thickening, one disc diameter or larger in size and located < one disc area from the center of the macula